

**REMARKS**

Claims 69-74 and 76-81 were pending in the present application. Claims 69-74 and 76-81 have been rejected by the Examiner. By virtue of this response, claims 69-74 and 76-81 have been cancelled and new claims 82-89 have been added. Support for the new claims is discussed below. No new matter has been added. With acceptance of the Amendment, claims 82-89 are pending in the application.

New claim 82 is the equivalent of cancelled claims 69 and 70, with additional language that, as discussed with Examiner Wilson in the Interview of July 12, 2004, places the claim in condition for allowance (see below). New claim 82, in addition to the verbatim pertinent language of cancelled claims 69 and 70, contains the limitation "wherein said nucleic acid sequence comprises a viral vector or portion thereof." New claims 83-89, which depend from claim 82, are verbatim equivalents of cancelled claims 71-74 and 76-78, which depended from cancelled claim 70. Support "wherein said nucleic acid sequence comprises a viral vector or portion thereof." is in the specification as filed at, for example, page 16, lines 18-22, and Examples IV and V. It was well-known at the time the application was filed that progeny of a cell transfected with a viral vector could contain a portion of the vector, rather than the entire vector. This is reflected in the language of the application as filed; see, e.g., page 7, lines 17-21: "An 'expression cassette or vector' is stably maintained in a hemopoietic or other cell type when it is either integrated into the chromosome so that the expression cassette or vector is replicated and transmitted to progeny cells . . ." [emphasis added]. This passage demonstrates that the entire vector is not necessarily replicated and passed into progeny cells, nor need the entire vector which contained the cassette, be replicated in order for progeny cells to express the desired gene product. Partial integration of viral vectors used at the time was well-known in the art. For partial retroviral vector integration, see, e.g., Coffin, *Retroviridae: The viruses and their replication*, in: Fields Virology, Fields, BN, Knipe, D.M., and Howley, P.M., eds, Third Ed., Lippincott-Raven, Philadelphia, 1996 (p. 1797, second column, last full paragraph, last sentence: "There is a loss of the appropriate number of bases from the end of the viral DNA [during integration] and a duplication of the correct number of bases of cellular sequence flanking the provirus." and p. 1799, #2: "The 3' terminal two bases at either end are removed [prior to integration] by the cleavage reaction of IN, leaving a 3'OH end."). References cited in support of

the above-quoted statements are: Chow *et al.* (1992) *Science* 255:723-6; Engelman *et al.* (1991) *Cell* 67:1211-22; Vink *et al.* (1991) *Nucl Acids Res* 19:6691-8; Brown *et al.* (1987) *Cell* 49:347-56; Fitzgerald *et al.* (1992) *J Virol* 66:6257-63; Kitamura *et al.* (1992) *Proc Natl Acad Sci USA* 89: 5532-6; Pryciak and Varmus (1992) *Cell* 69:769-80; Farnet *et al.* (1990) *Proc Natl Acad Sci USA* 87:4264-8; Fujiwara and Mizuuchi (1988) *Cell* 54:497-504; Lee and Coffin (1991) *J Virol* 64:5958-65. For partial integration of AAV, see, e.g., Giraud *et al.* (1995) *J. Virol.* 69:6917-24, e.g., at page 6922, second column, final paragraph ("Integration of less than a full genome equivalent of any of the recombinants characterized in this report does not require replication but does suggest that a circular molecule is an intermediate in the process.") and Rutledge and Russell (1997) *J. Virol.* 71:8429-36, e.g., at page 8429 ("[N]one of the vector proviruses integrated as intact, full-length genomes.") and at page 8435, final paragraph ("[E]ach AAV vector integration event is likely to produce a different, incomplete provirus . . ."). The quoted references are included herewith for the Examiner's convenience.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

In view of the preceding amendments and the remarks that follow, reconsideration and withdrawal of the outstanding objections and rejections is respectfully requested.

#### **Summary of July 12, 2004 and July 14, 2004 Interviews with Examiner Michael Wilson**

Applicants' representative Eric Witt wishes to thank Examiner Wilson for the courtesy and consideration extended to him in the telephonic interviews of July 12, 2004, and July 14, 2004, regarding the instant application and Office Action of May 18, 2004 (paper No. 051704). The remarks and questions of Examiner Wilson were very helpful in the preparation of this response to the Office Action.

In the Interview of July 12, 2004, proposed amended claim language was discussed. In particular, claim 70, and proposed amendments thereto, was discussed. Additional proposed claim

language “wherein said nucleic acid sequence comprises a viral vector or portion thereof” was discussed. Examiner Wilson stated that withdrawal of the rejection of claim 70 under 35 USC §112 as indefinite would be considered in light of the additional language. With this Amendment, Applicants cancel claim 69, from which claim 70 depended. Therefore, in order to place the application in condition for allowance, new claim 82, which merges old claims 69 and 70 and which contains the discussed language, has been added. Claims 71-74 and 76-79, which depend from claim 70, were discussed and their rejection based on the rejection of claim 70 was discussed. The Examiner stated that if claim 70 were acceptable, claims 71-74 and 76-79 would also be acceptable. Because claims 71-74 and 76-79 depended from claim 70, which depended from (now cancelled) claim 69, new claims 83-89, corresponding to claims 71-74 and 76-79 and depending from new claim 82, have been added in order to place the application in condition for allowance.

In the Interview of July 14, 2004, the reference McDonnell (Cell, 1989, 57:79-88) was discussed in relation to the rejection of claims 69 and 79-81 under 35 USC §102(b). No agreement was reached.

#### **Rejections under 35 U.S.C. § 112, second paragraph**

Claims 70, 72, 74, 80, and 81<sup>1</sup> stand rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. The Office Action states that rejections of claims 72 and 74 have been withdrawn (top of p. 3), and no new rejections of these claims are indicated.

The Examiner states in the Office Action (final paragraph, p. 2) that Claim 70 stands rejected because claim 69, from which it depends, does not require that the nucleic acid sequence was introduced into the cell. As suggested by the Examiner in the Office Action and modified in the Interview of July 12, 2004, Claim 70 (now claim 82) has been amended to include the language “wherein said nucleic acid sequence comprises a viral vector or portion thereof,” which does not

---

<sup>1</sup> Although the Office Action states, in the introductory sentence under Claim Rejections-35 USC §112, that claims 72 and 74 remain rejected, this appears to be an oversight, as rejections of claims 72 and 74 were withdrawn and no new rejections were stated. However, as discussed in the Interview of July 12, 2004, claims 71-74 and 76-79, although not specifically discussed as rejected in the present Office Action, appear stand rejected as dependent on claim 70, which remains rejected. This response will address therefore address these claims as well.

require that the nucleic acid sequence was introduced into the cell and thus, as discussed in the Interview, overcomes the rejection. New claim 82 corresponds to claim 70, written in independent form (in combination with claim 69, from which it depends, and which is cancelled with this Amendment), and with amended claim language reciting, "wherein said nucleic acid sequence comprises a viral vector or portion thereof," in order to place the application in condition for allowance. To make these changes clear, cancelled claims 69 and 70 and new claim 82 are presented below:

69. (cancelled) A pharmaceutical composition that induces tolerance to an antigen, said composition comprising a non-tumor lymphoid cell or non-tumor hematopoietic cell suitable for introduction into an individual and a pharmaceutically acceptable excipient, wherein said cell contains a nucleic acid sequence encoding a fusion protein operably linked to a promoter,

said fusion protein comprising (1) an immunoglobulin heavy chain or light chain; and (2) a polypeptide containing at least one epitope of the antigen;

wherein upon introduction to the individual said composition induces tolerance to the antigen in the individual.

Claim 70 (cancelled, with previous claim language and present claim language shown for comparison): The pharmaceutical composition of claim 69, wherein said nucleic acid sequence ~~was introduced into the cell in a viral vector~~ comprises a viral vector or portion thereof.

Claim 82 (new): A pharmaceutical composition that induces tolerance to an antigen, said composition comprising a non-tumor lymphoid cell or non-tumor hematopoietic cell suitable for introduction into an individual and a pharmaceutically acceptable excipient, wherein said cell

contains a nucleic acid sequence encoding a fusion protein operably linked to a promoter, wherein said nucleic acid sequence comprises a viral vector or portion thereof,

said fusion protein comprising (1) an immunoglobulin heavy chain or light chain; and (2) a polypeptide containing at least one epitope of the antigen;

wherein upon introduction to the individual said composition induces tolerance to the antigen in the individual.

New claim 82 excludes the phrase in claim 70, "The pharmaceutical composition of claim 69," but is otherwise a verbatim combination of claims 69 and amended claim 70. With this amendment, claim 69 is cancelled (see below) and new claim 82 is added in order to place the claims in condition for allowance. New claims 83-89, which depend from claim 82, are verbatim equivalents (with claim number from which they depend changed to reflect new claim 82) of cancelled claims 71-74 and 76-78, which depended from cancelled claim 70. As these claims depend from claim 70 and have no other outstanding rejections, if claim 70 (now claim 82) is allowable, claims 71-74 and 76-78 (now claims 83-89) are also allowable.

In view of the amended claim language, which was discussed in the Interview and which the Examiner has stated would be acceptable, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. §112, second paragraph.

#### **Rejections under 35 USC § 102(b)**

Claims 69 and 79-81 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by McDonnell et al. (Cell (1989) 57:79-88). Without acquiescing to the rejection, and solely in the interest of expediting prosecution, claims 69 and 79-81 have been cancelled, rendering this rejection moot. Applicants respectfully request that this rejection be withdrawn.

#### **Double Patenting**

Applicants acknowledge the withdrawal of the objection to claim 75 under 37 CFR 1.75 as being a substantial duplicate of claim 70.

Claim 81 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 69. Without acquiescing to the objection, and solely in the interest of expediting prosecution, claims 69 and 79-81 have been cancelled, rendering this objection moot. Applicants respectfully request that this objection be withdrawn.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 308072000110. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 19, 2004

Respectfully submitted,

By 

Eric H. Witt

Registration No.: 44,408  
MORRISON & FOERSTER LLP  
755 Page Mill Road  
Palo Alto, California 94304  
(650) 813-5755

Attachments